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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,156	TAGUCHI ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on June 18, 2008 is acknowledged. Claims 1-6 are pending in this application.

Restriction

1. Applicant's election of species alkali-solubilized collagen for biodegradable polymer, DMSO for the organic solvent, tri-carboxylic acid for different hardening component, succinimidyl for the "different hardening component", soft and soft tissue for types of tissue, and hemostatic from intravascular material in the reply filed on June 18, 2008 is acknowledged. It appears that succinimidyl should be elected from the electron-attracting group (see claim 2). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The restriction is still deemed proper and is made FINAL in this office action. Claims 1-6 are examined on the merits.

TRADEMARK

3. The use of the trademark BERIPLAST P®, GRF-GLUE®, DERMABOND® have been noted in this application at paragraphs [0034]-[0036] of instant specification US 2006/0239958 A1. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Objection

4. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 is drawn to a two-component, bio-degradable/absorbable adhesive medical material comprising a bonding component consisting of a solution containing a biodegradable polymer and either one of an organic solvent, water and a mixture of water and an organic solvent, and a hardening component consisting of a low-molecular weight derivative." The latter part of claim 1 is a "product by process" claim, and it will be examined as a product claim. The MPEP states the following: "[Even though product-by-process claims are limited by and defined by the process determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process...The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal

carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product" (see MPEP 211 [R-1]).

Rejection-35 U.S.C. 112, 2nd

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 recites, "...a bonding component consisting of a low-molecular-weight derivative..." It is unclear what is encompassed within the low-molecular-weight derivative. For example, it is unclear what types of modifications of the low-molecular-weight are encompassed with the derivatives. Because claims 2-6 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

8. Claim 1 recites, "...low-molecular-weight derivative..." It is unclear what these compounds are since the lower and the higher limits of what constitutes a low-molecular weight derivative is not defined in the specification.

Rejection-35 U.S.C. 112, 1st

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a two-component, bio-degradable/absorbable adhesive medical material comprising a bonding component

consisting of a solution containing a biodegradable polymer and a hardening component consisting of a low-molecular-weight derivative. The generic statement a hardening component consisting of a low-molecular-weight derivative does not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can form peptide or amide bonds, and make up the class of low-molecular-weight compounds. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives, variance and homologs. The specification is void of organic molecules that functions as a peptide-like molecule

that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules that can form peptide or amide bonds, and other synthetic peptide or peptide-like molecule and peptidomimetics or amino acid mimetics that can form low-molecular-weight compounds.

The specification discloses that a low-molecular weight derivative is prepared by modifying a carboxyl group in a di- or tri-carboxylic acid of the citric acid cycle, with an electron-attracting group (one or a combination of two or more selected from the group consisting of a succinimidyl group, a sulfosuccinimidyl group, a maleimidyl group, a phthalimidyl group, an imidazolyl group, a nitrophenyl group and a tresyl group, and derivatives thereof) (see abstract). The specification discloses that a biological low-molecular-weight derivative serves as a hardening component (see paragraph [0001] of instant specification US 2006/0239958 A1). Further, the specification discloses that "a biological low-molecular-weight derivative to be used in the present invention is prepared by introducing an active ester into the di- or tri-carboxylic acid of the citric acid cycle through the reaction between the di- or tri-carboxylic acid, and an electron-attracting group (see paragraph [0019] of instant specification US 2006/0239958 A1)...low-molecular-weight derivative may be obtained by adding a molecule serving as an electron-attracting group to an organic solvent solution of the di- or tri-carboxylic acid of the citric acid cycle, under the presence of a condensing agent, such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, and purifying an obtained product by silica-gel column chromatography (see paragraph [0020]). The working example only describes the citric acid derivative (CAD) as the biological low-molecular-weight derivative (see

paragraph [0029] and Inventive Examples 1-4). The specification discloses comparative examples (Examples 1-3) where BERIPLAST P®, GRF-GLUE®, and DERMABOND® were used to compare the bonding strength of each biological tissue adhesive (see paragraphs [0034]-[0038]). The specification discloses that "as seen in Table 2, while the biological tissue adhesive in Inventive Example 4 using CAD is inferior to Comparative Example 3, it has a higher bonding strength than those of the biological tissue adhesives in Comparative Examples 1 and 2" (see Table 2). The specification does not describe the structures of CADs. A low-molecular-weight compound can be any compound, since the lower and higher limits of the molecular weights are not disclosed. Any peptide, protein, organic molecules that are biologically active can be a low-molecular-weight derivative. Description of citric acid derivative is not sufficient to encompass numerous other peptides, proteins and other biologically active molecules that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. For example, if the low-molecular weight compound has a molecular weight of 10,000 Daltons, and if an average weight of an amino acid has 135 Daltons, then 10,000/135 = 74.07 amino acid residues. There are 20 naturally occurring amino acids, thus, this implies that there are $75^{20} = 3.17 \times 10^{37}$ different sequence possibilities for the low-molecular-weight compound. When the non-natural amino acids (such as D-isomers, b-amino acids, g-amino acids, e-amino acids, and protected amino acids) are factored into the equation, there are innumerable numbers of possibilities for the low-molecular-

weight derivative. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

35 U.S.C. 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Linden et al (US Patent No. 5,634,936).

13. Linden teaches a device for closing off a septal defect including a polymeric self-hardening material in a specific conformation which is delivered directly to a cardiac tissue or into a balloon which spans both surfaces of the defect, and hardened in-situ by

change in pH or ionic concentration, organic solvents (see abstract). Linden teaches biodegradable polymer that are collagen or poly-L-lysine which precipitates above a pH of 3.0. Linden teaches that polymers such as low molecular weight poly-L-lactic acid are soluble in DMSO and would precipitate on replacing the water miscible DMSO with water or saline solutions (see column 6, lines 46-51), meeting the limitation of claims 1-6. Linden further claims an apparatus for closing off a septal defect (see claims), a plug that meets the limitation of a sealant or blood vessel embolizing material of claim 6. Please note that the latter part of claim 1 is a "Product by Process" claim. The MPEP states the following: "[Even though product-by-process claims are limited by and defined by the process determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process...The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product" (see MPEP 2113 [R-1]). Please note that the intended use of claim 5 has not been given any patentable weight, since they do not further limit the compound.

14. Claims 1-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuda et al (JP 09-103479, as filed with IDS; translated version enclosed of the full document).

15. Matsuda et al teach a less toxic crosslinking method and a medical material formed by this method. The medical material is formed by crosslinking gelatin by succinimidized poly-L-glutamic acid. Matsuda teaches the method of mixing an aqueous solution containing the gelatin and an aqueous solution containing the succinimidized poly-L-glutamic acid and crosslinking the gelatin and the succinimidized poly-L-glutamic acid. Furthermore, the material is a medical material, such as vital adhesive, hemostatic material, embolous material for blood vessel and sealant of aneurysm which is used by direct crosslinking on medical treatment site (see abstract). The working example 1 discloses the method of making the gelling reaction with Poly-L-glutamic acid and gelatin in buffer solution (see paragraph [0006]) and the n-hydroxysuccinimide, poly-L-glutamic acid and a 1-ethyl 3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) were mixed and melted in DMSO. Since claim 1 recites, "a bonding component consisting of a solution containing a biodegradable polymer and either one of an organic solvent, water and a mixture of water and an organic solvent…", and buffer solution comprises of water and salts, this meets the limitation of claims 1-3 and 5-6. Please note, the intended use of claim 5 has not been given any patentable weight, since they do not further limit the compound.

Obviousness Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

17. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

18. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-5 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4 and 6-7 of copending Application No. 10/527,694 (US 2006/0128948 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because if one practiced the claimed invention of the instant application, one would necessarily arrive at the claimed invention of the copending application and vice versa.

20. Instant claims 1-5 are drawn to a two-component, bio-degradable/absorbable adhesive medical material comprising a bonding component consisting of a solution containing a biodegradable polymer and a solvent or water or mixture of both, and a hardening component consisting of a low-molecular-weight derivative.

21. Co-pending claims 4 and 6-7 are drawn to a crosslinked high-molecular-weight product obtained by crosslinking a high-molecular-weight compound with a biological low-molecular-weight compound, the crosslinked high-molecular-weight product comprising a gel that is metabolized in vivo after application in vivo, wherein the high-molecular-weight compound is at least one of glycosaminoglycans, chitosans and polyalcohols, and wherein the biological low-molecular-weight compound is obtained by modifying at least one carboxyl group of malic acid, oxalecetic acid, citric acid, or cis-asconitic acid with N-hydroxysuccinimide or N-hydrosulfosuccinimide.

22. The bonding component of the instant application consists of at least one of glycosaminoglycan and the low-molecular-weight-derivative are the same as the co-pending application, therefore, if one practiced the claimed invention of the instant application, one would necessarily achieve the claimed invention of the copending application 10/527,694 and vice versa.

23. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

24. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. H./
Examiner, Art Unit 1654

/Anish Gupta/

Primary Examiner, Art Unit 1654